CLINICAL EVALUATION OF SUSPECTED MOLD NEUROTOXICITY

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ABSTRACT

Doctors and forensic scientists are increasingly being challenged to evaluate individuals with mold exposure for health injuries, such as neurotoxicity. A significant body of research, described below, shows possible mold neurotoxic effects. Individuals presenting with neurotoxicity can be effectively evaluated with a standard neuropsychological evaluation, as follows. A 47-year-old married nurse, exposed to numerous molds over a 10-year period, with periods of peak exposures, became ill with multi-system symptoms, referable to respiratory, autonomic and central nervous system function. Carpeting dust analysis over various locations in the office showed elevated mold levels, including *Stachybotrys*.

Work and home history did not indicate mold or other neurotoxic substance exposure, other than mold from office. Immune function testing found elevated antibodies to Stachybotrys and other molds. Neuropsychological testing found deficits in working memory, processing speed, word fluency, manual dexterity, visual perception and executive function. Emotional function and personality were generally within normal limits. Although evaluated by many medical specialties, no competing diagnosis was found, resulting in a probable diagnosis of mold neurotoxicity.

INDEX TERMS: Adverse effects, mycotoxins, neurotoxicity, neuropsychology, toxic mold

INTRODUCTION

Objective: To show diagnostic procedures for analyzing an individual case with suspected mold neurotoxicity affecting central nervous system function.

Mycotoxins are formed by the hyphae and spores of common molds growing under a variety of conditions. Other prominent compounds include volatile organ-

ic compounds (VOC's), alcohols and aldehydes – these are not mycotoxins, although with sufficient concentration, they could have neurotoxic effects. Mycotoxins and possibly other by-products may be responsible for symptoms of headache, dizziness, and eye and mucous membrane irritation among individuals in fungus-contaminated buildings (Levetin, 1995).

Mycotoxin exposure at doses capable of producing chronic disease are usually far below those responsible for acute effects (Samson, 1992). Some are "neurotoxins, which in low doses may cause sustained trembling in animals, but at only slightly higher doses cause permanent brain damage or death" (Samson, 1992).

Case reports and other medical evidence of mold neurotoxicity: Johanning and Landsbergis (2001) reported that a majority of patients with fungal exposure had at least three nervous system complaints (such as headaches, nervousness, concentration problems, dizziness, and excessive fatigue) with 77 percent reporting at least one CNS symptom. Chronic fatigue was found in 50% of the subjects. Craner (2001) reported neuropsychological symptoms following mold exposure, including a case where the subject developed "marked behavioral changes, difficulty concentrating and short-term memory impairment, and profound fatigue," with neurocognitive impairment persisting after removal from the contaminated house. Auger (2001) reported four cases of chronic toxic encephalopathies apparently related to exposure to toxigenic fungi. Sigsgaard (2001) reported neurological and neuropsychological symptoms increasing with the number of hours spent in a damp building. The symptoms included headache, tiredness, and sleeping difficulties. Gordon (2001) studied twenty people who reported cognitive changes following exposure to fungi. All subjects were found to be neuropsychologically impaired on at least one measure, with 65 percent of the sample meeting three or more of the impairment criteria.

In summary, there is significant support in the scientific literature (including descriptions of mechanisms, group studies, and individual neuropsychological evaluations) for diagnosing individual cases of fungal/mold neurotoxicity. In the past, neuropsychological analysis has been helpful for the diagnosis of individual cases with numerous types of neurotoxic substance exposures (Singer, 1990; Singer, 2003a; Singer, 2003b).

METHODS

A standard neurobehavioral toxicology protocol was utilized, including extended history-taking, record review, and neuropsychological testing.

Subject: A 47 year old white woman, with 16+ years of school and a B. S. in Nursing, married with 5 children, was referred by her doctor for further evaluation

following mold exposure and subsequent illness. She was unemployed and in a worker's compensation case. Her main symptoms were deteriorated memory, concentration and learning skills; difficulty with multi-tasking; fatigue; and need for excessive sleep (10 hours per night). She was examined 8 months after workplace exposure ceased.

Exposure and symptoms: The subject worked a 40-hour week from June 1991 through February 2001 as a visiting nurse, spending 3-5 hours per day in the same office. She brought materials and clothing from the office to her car to visit clients on a daily basis. In 1994, after office renovations, there were plumbing and roofing leaks, resulting in sagging ceiling tiles. Buckets were placed to catch further precipitation from the ceiling, with the area blocked off with chairs. Although the exterior roof underwent various repairs, the roof continued to leak, and there was no remediation of the water from the roof, affecting the interior ceiling, walls, or carpet. The roofing leaks began to spread in the office with repeated water intrusions.

In 1995, the subject began experiencing bladder incontinence, fatigue, numbness and tingling of her heels and face, leg twitching at night, and dizziness, which occasionally progressed to true vertigo. She then developed bowel incontinence. She was examined by numerous medical specialists, who found no medical cause for her condition. She began to have significant fatigue all the time, with frequent bouts of colds and influenza. The symptoms continued through 1999, at which time the room in her office that had been blocked off because of leaks was reopened and reconnected with the general offices. All of the office and patient supplies were placed in this room, and conferences, staff meetings, and in-service meetings were held there, so there was significant potential exposure to this patient when she was in this room. In 2000, her desk was placed next to the open doorway of this room. She quickly and progressively became more ill, with confusion, and was in three mild automobile accidents (with no head trauma) within three months. She developed a chronic sinus condition, with a bronchial cough. She felt better on the weekends. Other coworkers also were reportedly sick, at least one with blood indicators of mold exposure, such as those of Stachybotrys exposure.

In January 2001, elevated levels of molds were found in the office (see below). The staff moved their own office supplies to another office, which had been vacated and remodeled because of toxic mold problems. In February, her condition worsened, with significant difficulties in automobile driving and concentrating, so she asked for medical leave.

RESULTS

Environmental testing: On 1/5/2001, fungal air and surface testing of the facility was conducted. The employees in the problem building surveyed their symp-

toms, refused to work in the contaminated building, and presented the results, which were included in the environmental testing report. The most common complaints among co-workers, all nurses or other health care workers, were respiratory difficulties, headaches, sleepiness, decreased concentration, sluggishness, irritability, anxiety, and mental sluggishness. Other reported symptoms included muscle twitching and jerking, clumsiness and incoordination, extreme sensitivity to odors and light, nosebleeds, and burning itchy eyes and skin.

The left half of the floor in the women's rest room was 80-100 percent saturated with water; the other half of the floor was at 20-40 percent relative saturation. The ceiling tiles were stained in the locations where roof leaks were reported. The environmental survey revealed that substantial quantities of Stachybotrys and other mold spores and contaminated dust were released during the demolition/construction work.

Carpet dust composite analysis: This method is expected to reflect a relatively long-term "record" of particles that have been airborne in the offices, and is thought to be the best single record of the levels of exposure throughout the office over the time that the subject was present. The sample was collected as a composite on one occasion, with some of the dust drawn from the carpet in several locations around the office which would normally be difficult to reach with a vacuum cleaner and might therefore be long-term repositories of dust

Table 1. Carpet dust composite analysis

Fungus type	Non-viable counts per 100 mg of carpet dust
Stachybotrys	200
Aspergillus/Penicillium	400
Cladosporium	600
Basidiospores - phaeo	700
Summary total	3200

Medical testing results: Brain MRI and NCV were reported as normal. Based on reports of numerous medical specialists, no medical cause of her illness has been confirmed, other than the fungal exposure. Significant fungal antibodies were found in the subject's blood, as follows (all units are reported as ELISA by Immunosciences Lab, Inc.):

Table 2. Fungal and myelin antibody testing

Date	Type	Result	Norms
11/28/00	IgG *Stachybotrys*	3100	0-1600
11/28/00	IgG *Cladosporium herbarum*	5500	0-1600
11/28/00	IgG *Pullularia pullulans*	4900	0-1600
4/10/01	IgM Myelin basic protein	55	0-50
7/17/01	IgG *Penicillium notatum*	4500	0-1600
7/17/01	IgG *Pullularia pullulans*	3300	0-1600
7/17/01	IgG *Stachybotrys*	2100	0-1600

Neuropsychological testing results

Symptom Testing: Positive on the Neurotoxicity Screening Survey (Singer, 1990), which assesses the consistency of responses to that of subjects with diagnosed neurotoxicity.

Cognitive and Executive Function Testing: The subject was tested on two occasions by different neuropsychologists (using different tests), as she sought further consultation from a neurotoxicologist. The significant findings are as follows:

Pre-exposure IQ[1]	95th percentile
WAIS-III Working Memory	25th percentile
Processing Speed	32nd percentile
WMS-III Auditory	47th percentile
WMS-III Auditory Delayed	42nd percentile
WMS-III Visual Delayed	58th percentile
WMS-III General Memory	58th percentile
Controlled Oral Word Association Test	10th percentile
Grooved Pegboard Test	8th and 9th percentiles
Paced Auditory Serial Addition Test	<1st percentile
Benton Visual Retention Test	Indicates Acquired Impairment
Stroop Color and Word Test	4th percentile (Color/Word)
Army Trail Making Test, part B	21st percentile
Visual Search and Attention Test	1st percentile

Emotional Testing: Emotion was within normal limits, as measured on six scales of emotional function.

Distortion and Malingering Testing: Based on nine negative indicators, as well as her social history, malingering is unlikely to be a significant factor.

Personality Testing: Using the Neo Personality Inventory Revised, and comparing the results with her social history, the subject was found to probably have a deterioration of personality, although definite abnormality was not reached.

DISCUSSION AND CONCLUSION

With regard to time- or concentration-dependent exposure indicators of mold exposure, scientists cannot intentionally expose people to mold, mycotoxins and other products of damp buildings, while constantly monitoring levels of exposure, in order to have an exact determination of exposure, because that would be unethical. Therefore, the carpet samples and biomarkers provide some of the best possible indicators of exposure.

The excessive antibody production to multiple toxic molds found in the patient's blood probably means excessive exposure, especially in light of the patient's severe symptoms. In addition, the composite carpet sample provided a good indicator of long-term exposure. The carpet sample would reflect the chronic exposure; however, there were periods of acute exposure resulting from building renovations releasing mold spores and mold parts, of which we have no specific environmental measurements, as is probably always the case; measurements are almost never considered until after people have become seriously ill.

The immune function testing found elevated antibodies to many of the same excessive levels of molds identified in the carpet sample. These molds were capable of producing the symptoms found, based upon the literature cited in this report.

The findings are most consistent with mold neurotoxicity. The subject reported no occupational or household exposure to pesticides, neurotoxic substances, no head injuries or other serious injuries, or diagnoses of psychiatric disorders. It is unlikely that the results reflect senile dementia, as her vocabulary and reasoning skills (which deteriorate with dementia) were at the 95th percentile, and the onset of symptoms was at age 39. Depression was ruled out by the Beck Depression Inventory. No competing diagnoses were found in the extended medical record. Brain MRI was normal, ruling out stroke, tumor, etc. Other workers were reported to be ill with symptoms resembling mold toxicity, by self report. The proposed method has provided substantial evidence, within reasonable scientific certainty, that the subject's central nervous system has deteriorated following extended exposure to various molds.

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